## **ABSTRACT**

The present invention relates to methods and compositions for the elucidation of gene function and the identification of novel genes. Specifically, the present invention relates to methods and compositions for improved functional genomic screening, functional inactivation of specific essential or non-essential genes, and identification of genes that are modulated in response to specific stimuli or encode recognizable phenotypic traits. In particular, the compositions of the present invention include, but are not limited to, expression cassettes comprising a novel polymerase primer hairpin linker that allows rapid construction of a single transcriptional unit encoding both strands of a hairpin siRNA, regardless of sequence. In addition, the present invention includes libraries comprising the expression cassettes of the invention, including vectors for transforming cells, such as replication-deficient retroviral vectors. The invention also includes methods for the production and screening of siRNA libraries, as well as therapeutic uses for the siRNAs expressed in accordance with the invention.

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